REMARKS

Support for the amendments

The claim amendments and new claims are fully supported in the application as filed, and thus do not constitute new matter. For example, the amendments to claim 4 are supported at page 3, paragraph 6, lines 2-4. New claims 8-12 are supported, for example, at page 3 paragraph 6 and page 4 paragraph 7.

Claim rejections under 35 U.S.C. § 102(b)

The Office Action rejected claims 4-7 under 35 USC § 102(b) as anticipated by US 6,132,711. The Applicant traverses this rejection, but nonetheless have canceled claim 7 and amended claims 4-6 to obviate the rejection.

In order to anticipate, a reference must teach each claim limitation, either explicitly or inherently. US 6,132,711 provides no teaching, either explicit or inherent, regarding administering allene oxide synthase to a subject at risk of ischemic injury as recited in claim 4, nor does it teach the limitations of the claims dependent on claim 4. Thus, the reference is not a proper anticipatory reference and the Applicant respectfully requests reconsideration and withdrawal of the rejection.

Claim rejections under 35 U.S.C. § 103(a)

The Office Action rejected claims 1-6 under 35 USC § 102(b) as obvious by US 6,132,711. The Applicant traverses this rejection.

In order to establish a prima facie case of obviousness under 35 USC § 103(a), the Patent Office must demonstrate that those of skill in the art would find that the cited reference, alone or in combination with the general knowledge in the art, teaches or suggests all of the claim limitations, either explicitly or implicitly. A finding of obviousness also requires a reasonable expectation of success in the cited reference.

In the present case, the Patent Office's position appears to be that if a compound is known as an antioxidant, that it would be obvious to use the compound to treat or prevent ischemia. However, the Patent Office has provided no basis for this assertion. The Patent Office instead cites to a single paragraph in the background of the cited reference, which merely lists ***some*** antioxidants have been used to treat ischemia. In no

way can it be asserted that the cited reference would lead those of skill in the art to believe that it would be obvious that any antioxidant can be used to treat ischemia with a reasonable expectation of success. The cited reference also does not teach that allene oxide synthases are effective for treating ischemia, but instead simply teaches that allene oxide synthases are antioxidants; no experiments were performed *in vivo* or on isolated biological tissues, organs, or animals to test for beneficial effects against ischemia.

The Applicant is providing exemplary abstracts from papers in which a known antioxidant was found to be ineffective in reducing myocardial infarct size (Venturini et al., J. Thromb. Thrombolysis 1998 May; 5(2):135-141; Miki et al., Basic Res. Cardiol. 1999, June; 94(3):180-187)). These are being provided to highlight the fact that the Patent Office has failed to establish that those of skill in the art would find it obvious to use any antioxidant to treat ischemia, or to use allene oxide synthases to treat ischemia.

Based on the above, the Applicant respectfully requests reconsideration and withdrawal of the rejection.

Claim rejection for non-statutory double patenting

The Office Action rejected claim 7 for obviousness-type double patenting over claims 1-2 of US 6,132,711. Claim 7 has been canceled, thus obviating the rejection. Thus, the Applicant respectfully requests reconsideration and withdrawal of the rejection.

Claim rejections under 35 U.S.C. § 101

The Office Action rejected claims 4-6 under 35 USC § 101 as not supported by a credible utility, based on the assertion that "prevention" of ischemic injury is an incredible utility as requiring an absolute limitation. The Applicant has amended claim 4 to obviate the rejection, and thus the Applicant respectfully requests reconsideration and withdrawal of the rejection.

CONCLUSIONS

Applicant respectfully contends that all conditions of patentability are met in the pending claims and therefore respectfully requests allowance.

If believed to be helpful to expedite prosecution of the above-referenced application, the Examiner is invited to contact the undersigned representative by telephone at (312) 913-2106.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff LLP

Dated: 11/23/05

By: _____
David S. Harper, Ph.D.
Reg. No. 42,636

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1: J Thromb Thrombolysis. 1998 May;5(2):135-141. Related Articles, Links
SpringerLink FULL-TEXT ARTICLE

The Antioxidant, N-(2-mercaptopropionyl)-glycine (MPG), Does Not Reduce Myocardial Infarct Size in an Acute Canine Model of Myocardial Ischemia and Reperfusion.

Venturini CM, Flickinger AG, Womack CR, Smith ME, McMahon EG.

Cardiovascular Diseases Research Department, G. Searle & Co., Monsanto Company, St. Louis, Missouri.

Oxygen radical generation can be measured when blood flow is restored to previously ischemic tissue. Although several studies have suggested oxygen radicals contribute to lethal injury of myocardium after ischemia, other studies have failed to confirm this implication. Antioxidants, such as N-(2-mercaptoptopionyl)-glycine (MPG) and superoxide dismutase, have had inconsistent effects on lethal myocardial injury in animal models of ischemia and reperfusion. Many variables influence lethal myocardial injury in these models: time of ischemia, time of reperfusion, dose of antioxidant, myocardial oxygen demand, area at risk, collateral blood flow, and body core temperature. The purpose of this study is to test the effects of infusion of MPG on lethal reperfusion injury in a canine model of ischemia and reperfusion with these variables tightly controlled. The left anterior descending coronary artery of anesthetized dogs was ligated for 90 minutes and reperfused for 4 hours. MPG was infused (100 mg/kg/h) 15 minutes before the end of ischemia and throughout reperfusion. Core body temperature was closely monitored, and infarct size was adjusted to transmural myocardial blood flow during ischemia. MPG had no effect on infarct size or infarct size adjusted for changes in collateral blood flow. These data reinforce a general difficulty in demonstrating the effects of antioxidant therapies on lethal injury, even when closely monitoring covariates known to impact infarct size.

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1: Basic Res Cardiol. 1999 Jun;94(3):180-7.

Related Articles, Links

SpringerLink FULL-TEXT ARTICLE

Failure of N-2-mercaptopropionyl glycine to reduce myocardial infarction after 3 days of reperfusion in rabbits.

Miki T, Cohen MV, Downey JM.

Department of Physiology, University of South Alabama, College of Medicine, Mobile 36688, USA.

Recent studies have reported that prolonged infusion of N-2-mercaptopropionyl glycine (MPG), a diffusible antioxidant, could limit infarct size in dogs. However, there are no comparable studies testing this agent in other species. We examined the efficacy of MPG in a rabbit model of infarction. Rabbit hearts were subjected to a 30-min coronary artery occlusion. Infarct size expressed as a percentage of risk zone was determined by either triphenyltetrazolium chloride (TTC) staining after 3h of reperfusion (study 1) or by histology after 72 h of reperfusion (study 2). In study 1, 37 +/- 2.6% of the risk zone infarcted in the control group. Intravenous MPG at a rate of 100 mg/kg/h starting 15 min after the onset of ischemia and continuing until 1 h after reperfusion had no effect on infarct size (35.4 +/- 3.4% infarction). However, infusion of MPG until the end of reperfusion significantly reduced infarct size as measured with TTC to 17.2 +/- 2.5% ($p < 0.01$ vs. control group). In study 2, 48.6 +/- 4.0% of the risk zone infarcted in the control group. In the treatment group MPG was started as above and was continued for 4 h of reperfusion followed by an intramuscular injection at the termination of the intravenous infusion. No protection was seen after 72 h of reperfusion (43.8 +/- 2.1% infarction). These findings reveal that MPG at a dose and schedule that appeared to protect the dog heart could not effect sustained protection in the rabbit heart. TTC staining revealed that MPG appeared to have preserved viability for up to 3 h of reperfusion suggesting that failure may have been due to early withdrawal of the drug. Alternatively, early TTC staining may yield spurious results under conditions in which protection is dependent upon antioxidant or free radical scavenger treatment as has previously been suggested. It is concluded that MPG as administered in the previous canine studies does not limit infarct size in all species, thus raising a concern about MPG's potential efficacy in man.